REMARKS

I. OBJECTION TO THE SPECIFICATION

The specification was object to because a sequence was presented in the drawing but the sequence identifier was not included in either the drawing or the brief description and the sequence was not included in the sequence list.

However the nucleotide sequence listed in figure 3 is exactly SEQ ID NO: 1, the first sequence listed in the sequence listing. This first sequence listed in the sequence listing also includes the amino acid conceptual translation of the protein that the nucleotide sequences codes, i.e. SEQ ID NO: 2, the amino acid sequence of the EWS protein. This is exactly what is shown in fig. 3 together with the division of the nucleotide sequence into exons (note that "exons" are among the optional features that can be shown with a nucleotide sequence). The nucleotide sequence SEQ ID NO: 1 is a known sequence as noted on page 12, line 11, of the applicants' specification.

Thus there is no need to add an additional sequence to the sequence listing because fig. 3 only shows the information provided in SEQ ID NO: 1 and SEQ ID NO: 2 of the already filed sequence listing.

The specification was also objected to because the "LXXLL-motives" mentioned on page 8, line 23, was not provided with a SEQ ID NO or listed in the sequence listing.

Applicants respectfully traverse the requirement to provide a sequence listing for "LXXLL-motives". According to MPEP 1.821 (a) only nucleotide and/or amino acid sequences that are specifically mentioned in the specification need to be listed in the sequence listing and provided with a SEQ ID NO. The term "LXXLL-motives" is not a specific amino acid and/or nucleotide sequence according to applicants' understanding. Instead it is a "higher level" term, like protein or protein fragment (see the accompanying article by D. M. Heery, et al, which is filed with an IDS). The rules for sequence listing do not require, for example, an amino acid sequence of any known protein or protein fragment that is mentioned in a specification to be listed merely because the sequence of the protein is known. The same applies *mutates mutanti* to the "LXXLL-motives". The "LXXLL-motives" refer to a part of a protein and thus are in the same category as a named known protein or named known protein fragment; the rule does not require that an amino acid sequence must be provided for the LXXLL-motives. Furthermore "L" and "X" are neither nucleotides nor amino acids.

In addition the LXXLL-motives is not present in the EWS protein.

Also the term "LXXLL-motives" was not used in any previously filed or pending claims and is not essential to an understanding of the metes and bounds of the claimed invention. Also it is not essential for an understanding of the relationship of the claimed invention to the prior art.

Recently it has been held by the Federal Circuit Court of Appeals in *Capon v. Eshar*, Fed. Cir. No. 03-1480, August 12, 2005, that the written description requirement does not impose a rule that the specification must recite

a nuclotide sequence of claimed DNA when that sequence is already known. Note that in the present case the LXXLL motives are not even mentioned in the claims.

However applicants have noted that the proper internationally approved formula for indicating a sequence number for a sequence was not used in the original specification and for that reason the various paragraphs in the specification containing the designation of the sequence numbers were appropriately amended.

Also some minor errors, such as grammatical errors, in the wording of the specification were corrected. The single incorrect reference to SEQ ID NO: 1 on page 12 was corrected.

For the foregoing reasons and because of the changes in the specification withdrawal of the objection to the specification is respectfully requested.

II. OBJECTIONS TO THE CLAIM WORDING

Claims 3 and 6 have been amended by including the features and limitations of claim 1 in each of these claims. The preamble of canceled claim 1 has been used in the amended claims 3 and 6, but the term "substances" has been changed to "a test substance" as suggested on page 3 of the Office Action. The number of steps in claims 3 and 6 has not been increased because e.g. step a) of claim 3 and also claim 6 is simply a more detailed version of step a) of canceled claim 1. The wording of claim 6 has also been amended as suggested

on page 4 of the Office Action under the "objection" and also to avoid the rejection under 35 U.S.C. 112, first paragraph.

Claim 5 has been amended as suggested on page 4 of the Office Action.

Claim 17 has been canceled, obviating the objection to its wording.

Because the suggestions regarding the objectionable claim wording have been adopted in the amended claims, withdrawal of the objection to the claimed wording is respectfully requested.

III. REJECTIONS UNDER 35 U.S.C. 112, 1st paragraph

Claims 1 to 9, 14 to 18, 23 to 25 and 28 to 30 were rejected under 35 U.S.C. 112, first paragraph, for being based on a specification that does not enable one skilled in the art to make and/or use the invention claimed in these claims and for failing to comply with the written description requirement.

Claims 14 to 18, 23 to 25 and 28 to 30 have been canceled, obviating their rejection for lack of enablement.

Furthermore page 4 of the Office Action stated that the claimed the current specification **is enabling** for an in vitro method of determining the effect of a test substance on the binding or ligand-induced activity of EWS protein of SEQ ID NO: 2 or a fragment thereof comprising amino acids 319 to 656 and human androgen receptor or a fragment thereof including amino acids 325 to 918 (current specification indicates that the fragment should have amino acids 325 to 919 and the claims above use this range – see Fig. 1 and page 16, line 9 of

applicants' specification).

Claims 3 and 6 have been amended by including the features and limitations of claim 1 in each of them. The broad claim 1 has been canceled.

Also the independent method claims 3 and 6 have been further limited to subject matter enabled by the originally filed specification in accordance with page 4 of the Office Action, as stated above. The subject matter regarding HNF-4 however has not been included in the claims to avoid the cited prior art.

Basis for the change to an "in vitro" method involving "cells" in claims 3 and 6 is found on page 9, line 5, and page 10, lines 1 and 21, of applicant's specification.

Also a paragraph has been added at the end of each of claims 3 and 6 to establish the connection between determining the effect of a test substance on the binding or ligand-induced activity and hormonal effects of the test substance. In the case of claim 3 this added paragraph is basically the suggested paragraph on page 13 of the Office Action, which is necessary to overcome the indefiniteness rejection described hereinbelow.

A new dependent claim 31 has been added to claim preferred methods of measuring the protein-protein or protein-protein-DNA interaction of claim 31. These methods are well known in the biochemical arts. A detailed explanation of these methods should not be required in the present application. It is well known that what is old and well known in the art is better left out of a patent specification.

For example, the Federal Circuit Court of Appeals has said:

"[A] patent need not teach, and preferably omits, what is well known in the art". ***Hybritech Inc. v. Monoclonal Antibodies, Inc.***, 802 F. 2nd 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986).

This teaching of the Federal Circuit should also be applied regarding inclusion of nucleotide and/or amino acid sequences. If a protein of known amino acid sequence is mentioned in the application, applicants should not be required to specifically list or describe the amino acid sequence of that known protein.

Also note the recent decision in *Capon v. Eshar*, Fed. Cir. No. 03-1480, August 12, 2005.

For the foregoing reasons and because of the changes in amended claims 3 and 6, withdrawal of the rejections of amended claims 3 to 8 under 35 U.S.C. 112, first paragraph, is respectfully requested.

IV. REJECTIONS UNDER 35 U.S.C. 112, 2nd Paragraph

Claims 1 to 9, 14 to 18, 23 to 25 and 28 to 30 were rejected under 35 U.S.C. 112, second paragraph, for indefiniteness.

Claims 1, 14, 15, 29 and 30 have been canceled, obviating their rejection for indefiniteness.

Claim 3 has been amended to provide the suggested paragraph establishing the missing connection. The connection between the binding of a substance to e.g. the androgen receptor and hormonal effects of the substance,

such as androgenic or anti-androgenic effects, is well known in the art. For example see the first paragraph and other paragraphs on page 3 of the background section in applicants' originally filed specification. Also see page 9, lines 18 to 22, of applicants' originally filed specification regarding the scope of the term "hormonal effects".

Also the term "ligand-induced activity" is not used in any of the amended claims 3 to 8.

In addition, the term "reporter gene activity" in step b) of claim 6 does not lack antecedent basis because it has not previously been used in the claim.

For the foregoing reasons and because of the changes in the amended claims and the claim cancellations withdrawal of the rejection of amended claims 3 to 8 under 35 U.S.C. 112, second paragraph, is respectfully requested.

V. ANTICIPATION REJECTION

Claims 1 to 9 were rejected under 35 U.S.C. 102 (a) as anticipated by Araya, et al, published February 14, 2003.

Only amended claims 3 to 8 remain pending.

Araya, et al, does disclose effects of EWS binding on a "derivative" of AR, namely another nuclear receptor HNF-4.

First, the *intended* scope of "derivative" of e.g. AR would or should not include so many changes that one would arrive at another nuclear receptor protein irregardless of the broad definition on page 5 of the present application.

Second, of course the new claims 3 and 6 do not have a scope that encompasses the HNF-4 nuclear receptor. The scope of these claimed methods only includes exposing cells or transfixed cells *in vitro* to androgen receptor or a fragment thereof with amino acid sequence 325 to 919 together with EWS protein or the fragment thereof as claimed in claims 3 and 6.

As pointed out in the Office Action the results for binding experiments between androgen receptor and proteins whose sequence differs greatly from EWS protein or the claimed fragment of EWS protein that has substantially similar activity are not predictable. Particularly the nuclear receptor protein HNF-4 is not either the EWS protein or the claimed fragment of EWS protein.

Thus Araya, et al, does not disclose or suggest the subject matter of claims 3 and 6.

For the foregoing reasons withdrawal of the rejection of amended claims 3 to 8 as anticipated under 35 U.S.C. 102 (a) by Araya, et al, published February 14, 2003, is respectfully requested.

Furthermore it is respectfully submitted that none of the amended claims 3 to 8 should be rejected as obvious under 35 U.S.C. 103 (a) over Araya, et al, published February 14, 2003.

VI. OBVIOUSNESS REJECTION

Claims 23 to 25 were rejected as obvious over Araya, et al, published February 14, 2003 (IDS filed 8/4/2004) and further in view of Brown, et al, US

2003/0082511 A1.

This obviousness rejection has been obviated, by the cancellation of claims 23 to 25.

Both Brown and the specification of the above-identified U.S. Patent Application (currently claim 8) do teach that screening of test substances that modulate activity of target molecules, particularly nuclear receptors, can take place in a number of different host cells including epithelial cells and nerve cells.

Should the Examiner require or consider it advisable that the specification, claims and/or drawing be further amended or corrected in formal respects to put this case in condition for final allowance, then it is requested that such amendments or corrections be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing the case to allowance, he or she is invited to telephone the undersigned at 1-631-549 4700.

In view of the foregoing, favorable allowance is respectfully solicited.

Respectfully submitted,

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